CARDIOVASCULAR COMPLICATIONS OF SCORPION STINGS AND THE EFFECTS OF ANTIVENOM

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The study was designed to evaluate (1) the frequency and types of cardiovascular complications caused by scorpion stings and (2) the effects of cardiovascular morbidity and mortality caused by changes in antivenom policy instituted in mid-1991 from an optimal treatment of none or 1 ampoule to the current mandatory dosage of five or more ampoules administered at point of first contact. From January 1992 to December 1995, prospective clinical and echocardiographic observations were made on 179 of 968 cases of scorpion sting admissions who had cardiovascular complications. A retrospective analysis of deaths and of all cases of scorpion stings treated for pulmonary edema or cardiopulmonary arrest (among 162 admissions) in the two years preceding the policy change (January 1990 to December 1991) was also undertaken. Most patients in the preceding two years had received 0 to 1 ampoule of antivenom. In the prospective study, cardiovascular complications were observed in 179 (18.5%) cases. Electrocardiographic (ECG) abnormalities were most frequent (72%) and included sinus tachycardia (56%), tented T-waves (29%), non-Q infarct pattern (17%), Q-infarct pattern (3%); supraventricular tachycardia; atrial fibrillation; and second-degree AV block and nodal tachycardia in one patient each. Echocardiography obtained in 48 cases within 24 h of sting was normal in 23 (48%) but showed abnormal left ventricular systolic function in 25 (52%), including all 12 patients with pulmonary edema. Serial echoes in 14 abnormal cases showed significant improvements in ejection fraction from 36.7 ± 14.6% to 58 ± 11.4% (P = 0.00002) with corresponding significant changes in fractional shortening % (P = 0.00033) following therapy. Interventricular septal motion abnormality was most frequently seen, left ventricular posterior wall motion abnormality was less common, and global wall motion abnormality was seen only in the more severe cases. There was a reduction in the incidence of pulmonary edema from 11.1% to 1.2% (P < 0.001), of cardiorespiratory arrest from 7.4% to 0.4% (P < 0.001), and cardiac-related deaths from 1.8% to 0% (P < 0.001), respectively, since the new serotherapy schedule. All cardiovascular changes including ECG and echocardiographic, congestive heart failure, and pulmonary edema were reversible in survivors.

SCORPION STINGS are a major health problem in the Middle East, and a common medical problem in many other countries. In Mexico, there are about 300,000 stings with 1000 deaths per year. In Saudi Arabia, scorpion stings accounted for 1.1% of 179,800 total admissions from 1985 to 1995. There are 650 scorpion species worldwide, but only 2 species - Leiurus quinquestriatus ("yellow") and Nebo hierichonticus ("black") are common in the Al-Baha region of Saudi Arabia.

Cardiovascular and neurologic complications account for the most severe morbidity and are the leading causes of mortality in scorpion stings.
Mortality is much higher in children than in adults. In Brazil, deaths due to scorpion stings were 0.8% to 1.4% among adults, 3% to 5% among school children, and 15% to 20% among very young children. 1

Prior to 1991, there was no consensus on the use of scorpion antivenom in this hospital and region, and hence most patients received either none or 1 ampoule of antivenom. This policy was changed in mid-1991, and all patients with scorpion stings have since received five or more ampoules of antivenom (unless they were allergic). The initial dose was usually given immediately when the patient presented to the primary health center or hospital.

In a previous communication from this center, echocardiographic findings in scorpion stings had been documented in children.14 The present study was designed to evaluate echo cardiographic changes, the frequency of other cardiovascular manifestations of scorpion stings in all patients (children and adults), and the effects of the new antivenom dose and schedule on severe cardiovascular morbidity and mortality.

Patients and Methods

The present study was designed in two parts. The first part was a prospective study of 968 consecutive patients with scorpion stings admitted to King Fahd Hospital from January 1992 to December 1995. Complete blood count, electrolyte, urea and creatinine; cardiac and liver enzymes; chest x-ray; ECG; blood gas analysis; and coagulation profiles were done routinely in all admitted cases and were obtained in all scorpion sting cases with cardiovascular complications. We attempted to obtain echocardiographic studies on all patients with severe myocardial dysfunction, as manifested by pulmonary edema and ECG changes of Q and non-Q myocardial infarction patterns within the first 24 h of sting. We also randomly studied by echocardiography selected patients with normal ECG and those with milder ECG changes, such as isolated T-wave changes, within the first 24 h of sting. Echocardiographic studies were repeated if the initial studies were abnormal. The second part of the study was a retrospective analysis of a cases of pulmonary edema and cardiopulmonary arrest from scorpion stings among 162 consecutive case of scorpion stings admitted from January 1990 to December 1991. All cases of pulmonary edema or cardiopulmonary arrest complicating scorpion stings were usually admitted and treated in the intensive care unit. We compared the incidence of these two severe complications in 1990 and 1991 when none or 1 ampoule of antivenom was given with the incidence from 1992 to 1995 when five or more ampoules of antivenom were given.

Except for the changed policy on anti venom dosage, the treatment protocol for scorpion stings had not changed since 1985 in this hospital and the region. Analgesics were used as indicated. Acutely ill patients were managed in the intensive care unit. Frusemide, inotropics, chlorpromazine, and vasodilators were used as indicated and at the discretion of the treating physician. We made no attempts to interfere with the general management of each patient by individual physician.

Statistical Analysis

Statistical analysis employed the chi-square methods.

Results

Prospective Observations

Of the 968 cases admitted with scorpion stings, 179 (18.5%) had cardiovascular complications. The majority of patients with cardiovascular complications (67%) were below 15 years of age, and the same proportion were males (Table 1). A total of 81 (45.3%) cases were bitten by yellow scorpions (Leiurus quinquestriatus), 22 (12.2%) by black scorpions (Nebo hierichonticus), and 76 (42.5%) by unidentified scorpions.

The major constitutional symptoms manifested in the 179 patients included: vomiting (75%), sweating (67.5%), salivation (40%), priapism (48.3%), and fever (28%). Associated neurologic manifestations were observed in 55%, and 85% of these were younger than 15 years. Abnormal laboratory findings included leucocytosis in 68%, hyperglycemia in 51%, elevated creatinine kinase level in 55%, aspartate

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Male (no.)</th>
<th>Female (no.)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>42</td>
<td>28</td>
<td>70</td>
</tr>
<tr>
<td>6-10</td>
<td>21</td>
<td>9</td>
<td>30</td>
</tr>
<tr>
<td>11-15</td>
<td>15</td>
<td>6</td>
<td>21</td>
</tr>
<tr>
<td>16-20</td>
<td>10</td>
<td>2</td>
<td>12</td>
</tr>
<tr>
<td>≥ 21</td>
<td>34</td>
<td>12</td>
<td>46</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>122</strong></td>
<td><strong>57</strong></td>
<td><strong>179</strong></td>
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</tbody>
</table>

Table 1. Cardiovascular complications of scorpion stings (age and sex distribution of 179 patients).
aminotransferase in 44%, and lactate dehydrogenase in 25%.

The cardiovascular abnormalities are shown in Table 2 and include pulmonary edema (7%), transient hypertension (31%), and hypotension (17%); the latter two were adjusted for age. The ECG abnormalities include sinus tachycardia in 56%, tall and peaked T waves in 29%, significant ST depression or elevation (similar to non-Q infarct pattern) in 17%, and T inversión in 15% of cases, occurring singly or in various combinations (Figure 1). Six patients (3%) had abnormal Q waves; one each of another 4 patients had atrial fibrillation, supraventricular tachycardia, second-degree AV block, and nodal tachycardia. Five patients had premature ventricular contractions. Most abnormal ECG changes were corrected in 2 to 14 days, however, abnormalities persisted for up to 6 wk in one case.

All 12 patients with pulmonary edema, all 3 patients with Q-infarct pattern (without pulmonary edema), and 10 of 18 patients with non-Q infarct pattern were studied by echocardiography. For comparison, 7 of 30 cases with only T-wave anomalies, 15 cases with either normal ECG or with only sinus tachycardia, and 1 of 3 cases with either nodal or supraventricular tachyarrhythmias were also studied. A total of 48 cases were thus studied by echocardiography within 24 h of sting. Ejection fraction (EF) was normal in 23 (48%) and abnormal in 25 (52%). Systolic dysfunction was mild (EF, 46% to 55%) in 32%, moderate (EF, 31% to 45%) in 36%, and severe (EF<:; 30%) in another 32% of the 25 cases. In 14 of the 25 patients in whom the initial echocardiographic systolic functions were abnormal, serial echo cardiography was obtained. In this group, the mean EF had increased from 36.7 ± 14.6% to 58.4 ± 11.4% (P = 0.000022) with corresponding significant increases in fractional shortening (IFS), P = 0.00033 and interventricular septum thickness fraction percent (IVSTF %), P = 0.0128) (Figures 2 and 3). The posterior wall thickness traction percent (LVPWT %) in this group was not significantly changed, except in a subgroup of five patients whose posterior wall was found to be hypokinetic in the initial study but improved significantly (P < .01) in subsequent studies.

Echocardiography in all 12 patients with pulmonary edema showed moderate to severe left ventricular systolic dysfunction. Pulmonary edema was associated with ECG features of Q-infarct pattern in 3 cases, non-Q infarct pattern in 7, and sinus tachycardia with diffuse T-wave changes in 2 cases. EF was severely reduced (22 ± 8%) in three other cases with Q-infarct pattern. EF was normal in 20%, mildly, moderately, and severely reduced in 30%, 20%, and 30% of cases, respectively, with non-Q infarct pattern. Six of 15 cases with isolated T-wave changes and 14 of 15 cases with normal ECG/sinus tachycardia only had normal EF. One patient with isolated T-wave changes had mildly reduced EF, another with sinus tachycardia had moderately reduced EF (44%), and one patient with nodal tachycardia also had a moderate reduction in EF (43.1%).

The recovery time for clinical cardiovascular function ranged from 5 to 12 days in all patients. Full recovery of echo-derived functions was also usually rapid but lagged behind clinical functional recovery in a few cases. In one patient, echo-derived functional recovery took as long as 33 days. Four patients had cardiopulmonary arrest but were successfully resuscitated.

### Pulmonary Edema

A total of 30 patients developed pulmonary edema; 18 of 162 (11.1%) during January 1990 to December 1991 and 12 of 968 (1.2%) during January 1992 to December 1995. The majority of these cases (74%) occurred in patients younger than 15 years. When compared with the total population of patients with cardiovascular complications, those with pulmonary edema had a higher incidence of sweating (80% vs 68%), salivation (60% vs 40%), and priapism (63% vs 33%). Also, leucocytosis (93% vs 68%), thrombocytosis (50% vs 35%), hyperglycemia (86% vs 51%), elevated creatinine kinase (80% vs 55%), and lactic dehydrogenase (66% vs 25%) were more frequent in patients with pulmonary edema. Twenty of the 30 patients with pulmonary edema received full dose of antivenom of at least 5 ampoules. In 1990 and 1991, 10 patients with pulmonary edema had

### Table 2. Cardiovascular complications in scorpion stings: frequency distribution among J 79 patients.

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) ECG abnormalities</td>
<td>129</td>
<td>72</td>
</tr>
<tr>
<td>2) Hypertension</td>
<td>56</td>
<td>31</td>
</tr>
<tr>
<td>3) Hypotension</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>4) Echocardiographic abnormalities</td>
<td>52</td>
<td></td>
</tr>
<tr>
<td>5) Pulmonary edema/LVF</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>6) Cardiopulmonary arrest</td>
<td>7</td>
<td></td>
</tr>
</tbody>
</table>

LVF = left ventricular failure.
Figure 1: Electrocardiographic changes in Scorpion stings.

IA: A 12 lead ECG (14.7.93) of a 16 years old male showing tall T waves, which resolved later (20.7.93).

IB: 12 lead ECG of a 9 years old male showing ST segment depression in leads I, II, AVF and V1, V3, V4 & V5 and ST elevation with Q waves in leads I & AVL (10.7.90). A significant resolution of these changes is noted on a repeat tracing (18.7.90).

IC: A 12 lead ECG (27.8.93) of an 11 years old male showing QS pattern and convex ST segment elevation in leads V2 through V6 with poor R wave progression over these leads and subsequent resolution of most of these changes (6.9.93).
Figure 2. Echocardiographically derived ejection fraction, within the first 24 h and following treatment.
Figure 3: Echocardiographic indices of systolic functions. EF = ejection fraction; FS = fractional shortening; IVSTF = interventricular septal thickness fraction; LVPWT = left ventricular posterior wall thickness fraction.
received 0 to 1 ampoule of antivenom, and 8 had received 5 to 10 ampoules. However, from 1992, 12 of 12 cases of pulmonary edema had received 10 to 30 ampoules of anti venom. In 1990 and 1991, 12 (7.4%) patients had cardiopulmonary arrest; all required assisted ventilation and there were three deaths. All three deaths had received none or 1 ampoule of anti venom. None of the patients who received five or more ampoules of anti venom died. In 1992 to 1995, 4 (0.4%) patients had cardiopulmonary arrest and all four required ventilation; there were no deaths. There was a significant drop in the incidence of pulmonary edema (P < 0.001), cardiopulmonary arrest (P < 0.001), and death (P < 0.001) following the introduction of the current early/high-dose serotherapy.

Discussion

The findings in this study show 18.5% of patients with envenomation had cardiovascular complications and 10.2% had neurologic complications, supporting previous observations that cardiovascular complications were more frequent than neurologic complications.9 We did not encounter any patients during the prospective study period with serious neurologic complications who did not have some cardiovascular manifestations. The spectrum of cardiovascular complications that we encountered included electrocardiographic features simulating myocardial ischemia and infarction; other electrocardiographic changes such as sinus tachycardia, supraventricular arrhythmias, ventricular ectopies; sinus bradycardia, second-degree AV block, left ventricular systolic dysfunction, congestive heart failure, and pulmonary edema. Sinus tachycardia in 56% of cases was by far the most common cardiovascular abnormality. Supraventricular tachyarrhythmias and various grades of AV block were rare; they occurred in less than 1% of cases with severe envenomation. Our experience is similar to previous documentations in the literature.9-16 In this study, ECG features of Q-infarct pattern was associated with 100%, non-Q infarct pattern with 80%, T-wave changes alone with 14%, and sinus tachycardia/normal ECG with 7% incidence of cardiovascular dysfunction manifested by pulmonary edema and/or reduced EF on echocardiography. Normal ECG, sinus tachycardia, and T-wave changes generally suggested better ventricular function.

Almost all cardiovascular complications, including electrocardiographic and echocardiographic changes, were usually reversed with active management and had little or no residual abnormalities. This experience is similar to what has been previously documented.9-16 However, Brand et al, in 1988, has documented one case in whom severe echocardiographic and electrocardiographic abnormalities had persisted for longer than 4 mo.10 We encountered one patient in whom echo-derived systolic dysfunction had persisted for about 1 mo and another patient whose ECG abnormalities had persisted for 6 wk. All patients with pulmonary edema whom we studied by echocardiography showed moderate to severe left ventricular systolic dysfunction, thus confirming the cardiac origin of pulmonary edema in scorpion stings.17

Hyperstimulation of the sympathetic and parasympathetic nervous system has been documented in animals injected with scorpion venom.18-20 and high levels of circulating catecholamine have been reported in cases of scorpion sting.20.22 Sinus tachycardia, hypertension, hyperglycemia, and leucocytosis in our cases can be attributed to the direct effects of excess circulating catecolamine, whereas priapism, hypersalivation, sinus bradycardia, various grades of AV block in these cases were probably due to excess levels of circulating parasympathomimetics.23.24 The electrocardiographic localization of ischemia or infarct pattern was rarely limited to the territory of any particular major coronary artery. Hypokinesia on echocardiography was also rarely limited to the territories of the major coronary arteries. Interventricular septum was most commonly affected, left ventricular posterior wall was less common, but global hypokinesia was also noted in severe cases. Echo-derived indices of systolic function like EF %, FS %, IVSTF %, and LVPWT % were significantly reduced in all the severe cases but improved with treatment. We did not demonstrate echocardiographic features of diastolic dysfunction or increased contractility in any of the patients studied. Gueron et al, in 1980, found in dogs that scorpion venom was arrhythmogenic and increased left ventricular contractility, systemic arterial pressure, peripheral resistance, left ventricular end-diastolic pressure, and pulmonary arterial pressure.17 Although they found that cardiac output was reduced significantly in most experiments, the end-diastolic pressure and contractility increased. They attributed these changes to catecholamine-induced decreases in compliance.
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However, the findings in this study that ECG changes of Q and non-Q infarct patterns were most frequent in patients with pulmonary edema and in those with more severe systolic dysfunction, as shown by echocardiography, strongly suggest direct myocardial damage. Histopathologic changes reported in fatal cases of scorpion stings include degeneration and necrosis of muscle fibers, interstitial edema, and mononuclear infiltrates. These changes bear close similarities to conditions induced by large doses of catecholamines and phaeochromocytoma. All ultrastructural changes are transient and reversible in experimental animals. It is probable that some of the acute cardiac damage in these cases are due to the effects of excessive amounts of circulating catecholamine. Small doses of venom injected into the coronary arteries have been shown to cause positive inotropic effects, but not ultrastructural myocardial changes or spasms of a major coronary artery. While smaller doses of venom and smaller amounts of induced-catecholamine may increase contractility, it appears clinically that whenever significant ECG changes and cardiac symptoms occur, significant direct myocardial damage had already occurred.

The observations on pulmonary edema showed that this complication was most frequent in children younger than 15 years. These patients manifested the most severe general symptoms of envenomation and the most extensive myocardial damage, as detected by ECG and echocardiography. The current protocol of administering high-dose antivenom (five or more ampoules) very early was very effective in protecting against pulmonary edema (P < 0.001), cardiopulmonary arrest (P < 0.001), and cardiovascular deaths in scorpion envenomation (P < 0.001). Thus, scorpion antivenom not only reduces overall mortality but it also seems to prevent the severe toxic effects on the heart. Since cardiovascular toxicity is the most common serious complication of scorpion sting, this cardio-protection probably was critical to the significant reduction in mortality noted with early or high-dose antivenom.

Conclusions

Cardiovascular complications are the leading causes of severe morbidity and mortality in scorpion stings. The major cardiovascular complications include changes in blood pressure, reversible ECG abnormalities simulating myocardial ischemia or infarction, reversible echocardiographic changes of systolic dysfunction, and congestive heart failure/pulmonary edema. These cardiovascular manifestations appear to have been significantly decreased and modified by early or high-dose scorpion anti venom therapy.

References


